2. **AMENDMENT TO THE CLAIMS (LISTING OF CLAIMS):**

This listing of claims will replace all prior versions and listings of claims in the application:

1.   (Currently Amended)   A method of treatment of osteoarthritis, comprising the step of administering an effective amount of an inhibitor of a C5a G protein-coupled receptor to a subject in need of such treatment, in which the inhibitor is a compound which

    (a)   is an antagonist of a C5a G protein-coupled receptor,

    (b)   has substantially no agonist activity, and

    (c)   is a cyclic peptide or peptidomimetic compound of formula-I:
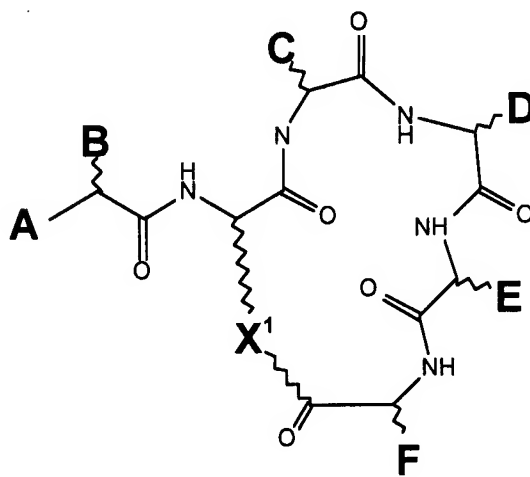
(I)

where **A** is H, alkyl, aryl, NH_2, NH-alkyl, N(alkyl)$_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$-alkyl, $NHSO_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B** is the side chain of ~~a D-~~ ~~or L-amino acid, but is not the side chain of glycine, D-phenylalanine,~~ ~~L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine~~ L-phenylalanine or L-phenylglycine;

C is the side chain of ~~a D-, L- or homo-amino acid, but is not the side chain of isoleucine,~~ ~~phenylalanine, or cyclohexylalanine~~ glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline;

D is the side chain of ~~a neutral D-amino acid, but is not the side chain of glycine or~~ ~~D-alanine, a bulky planar side chain, or a bulky charged side chain~~ D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;

E is ~~a bulky substituent, but is not~~ the side chain of ~~D-tryptophan, L-N-methyltryptophan,~~ ~~L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine,~~ ~~D-leucine, L-fluorenylalanine, or L-histidine~~ an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-napthyl or L-3-benzothienyl alanine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X^1 is -$(CH_2)_n$NH- or $(CH_2)_n$S-, where n is an integer of from 1 to 4; -$(CH_2)_2$O-; -$(CH_2)_3$O-; -$(CH_2)_3$-; -$(CH_2)_4$-; -$CH_2COCHRNH$-; or -$CH_2.CHCOCHRNH$-, where R is the side chain of any common or uncommon amino acid.

2. (Previously Presented) The method of claim 1, in which n is 2 or 3.

3. (Withdrawn) The method of claim 1, in which **A** is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.

4. (Withdrawn) The method of claim 2, in which **A** is a substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6 carbon atoms, or a phenyl or toluyl group.

5. (Withdrawn) The method of claim 3, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.

6.-9.   (Canceled)

10.   (Previously Presented) The method of claim 1, in which the inhibitor is a compound which has antagonist activity against C5aR, and has no C5a agonist activity.

11.   (Previously Presented) The method of claim 1, in which the inhibitor has potent antagonist activity at sub-micromolar concentrations.

12.   (Previously Presented) The method of claim 1, in which the compound has a receptor affinity $IC_{50} < 25$ μM, and an antagonist potency $IC_{50} < 1$ μM.

13.   (Currently Amended) The method of claim 1, in which the compound is selected from the group consisting of: compounds **1** to **6, 10** to **15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33** to **37, 39** to **45,** ~~47 to 50, 52~~**56** to **58** and **60** to ~~70~~**64 as follows:**~~described in PCT/AU02/01427.~~
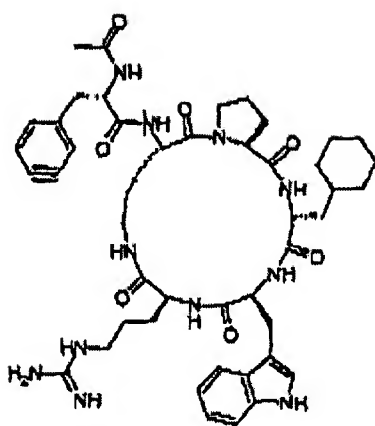
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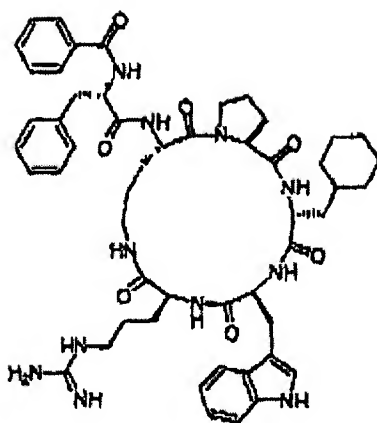
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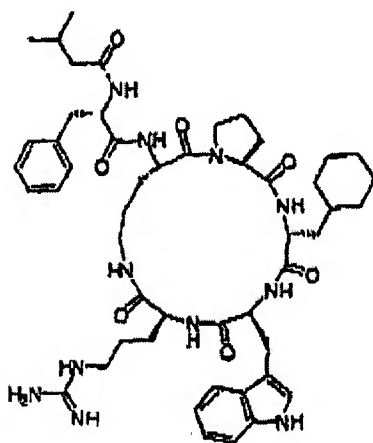
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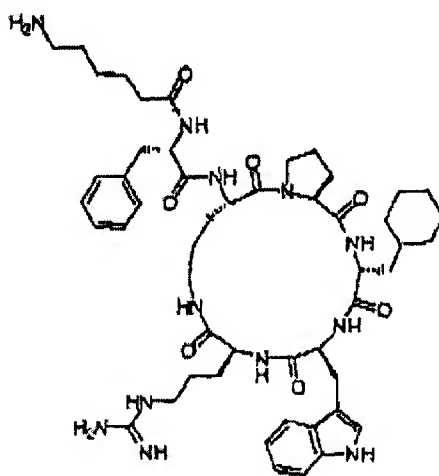
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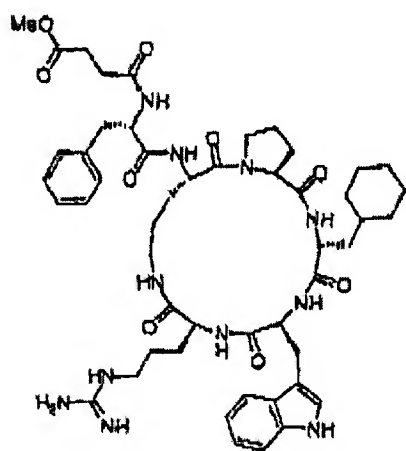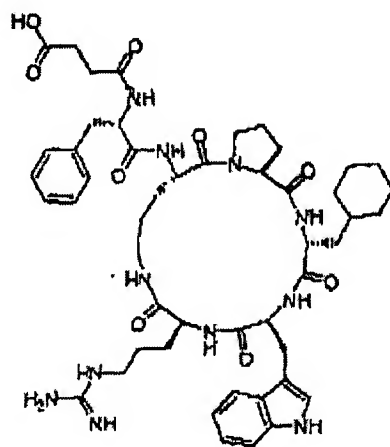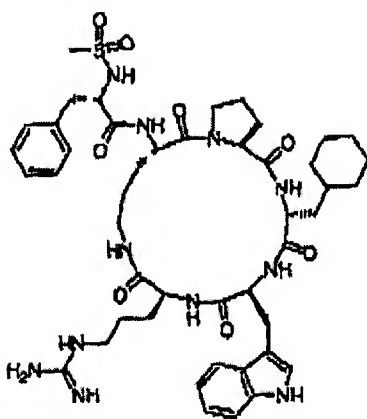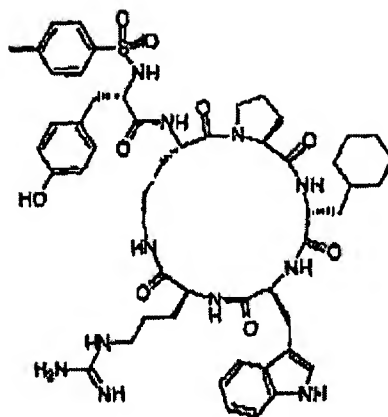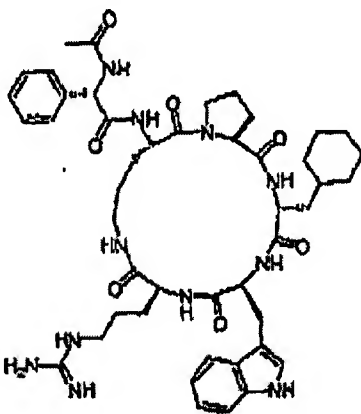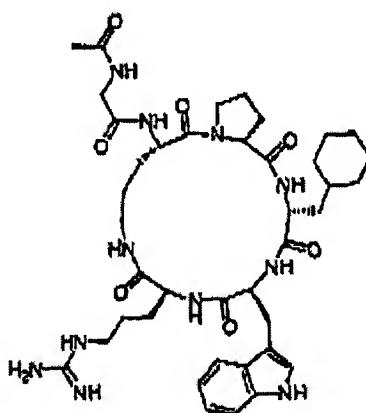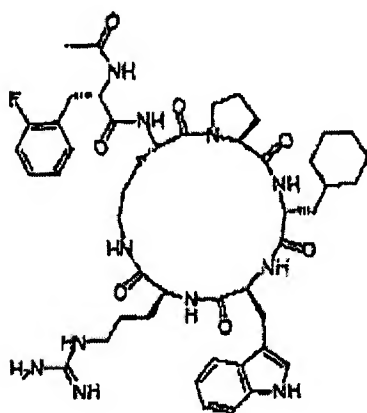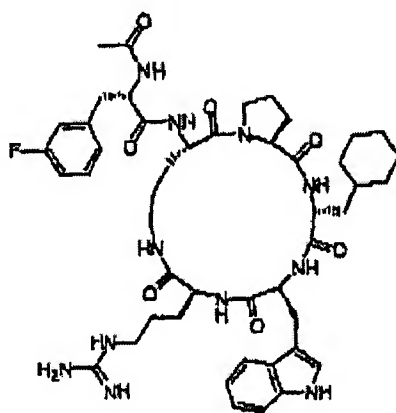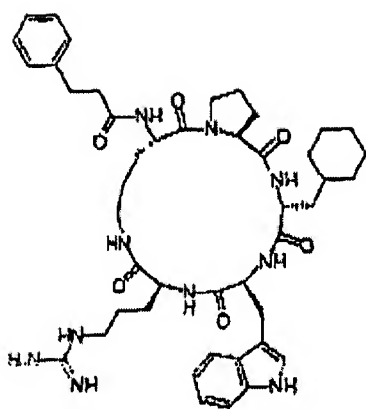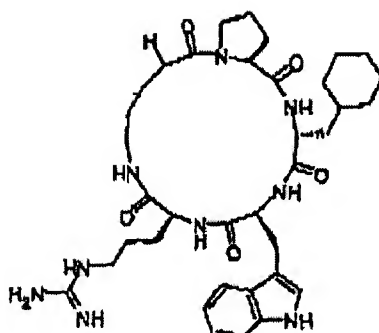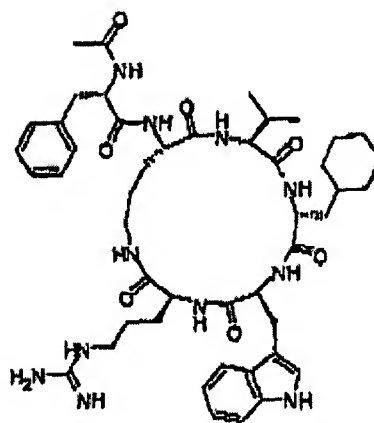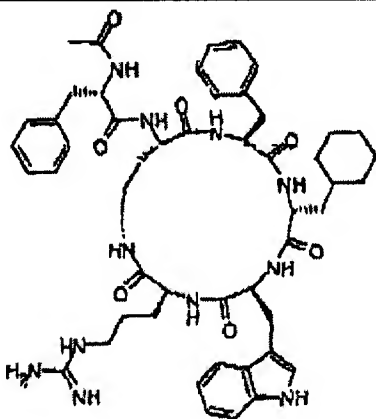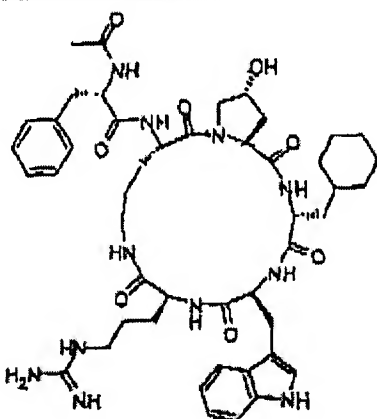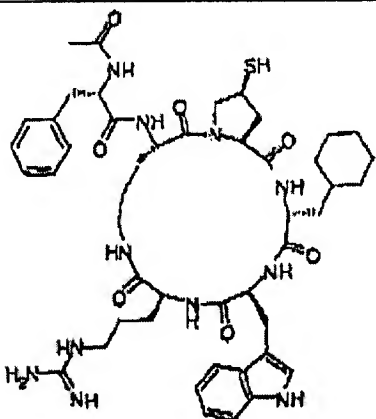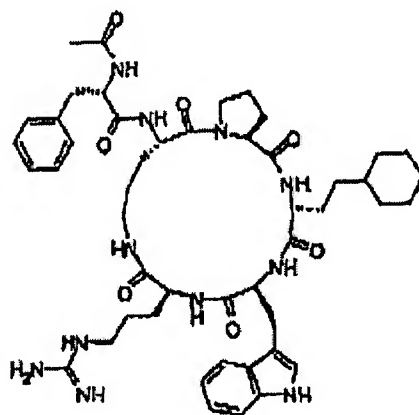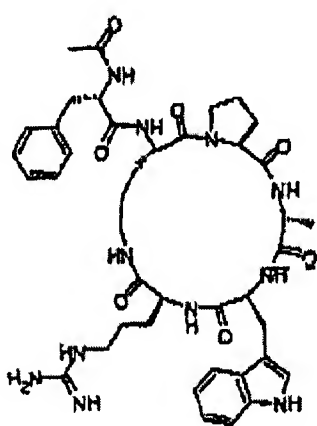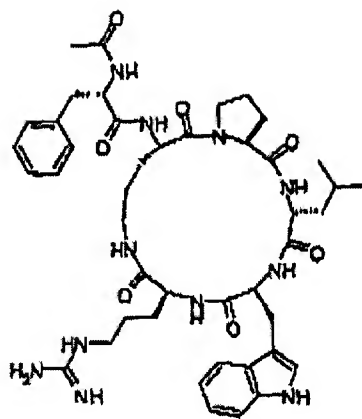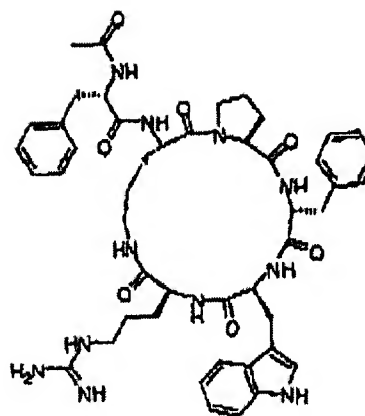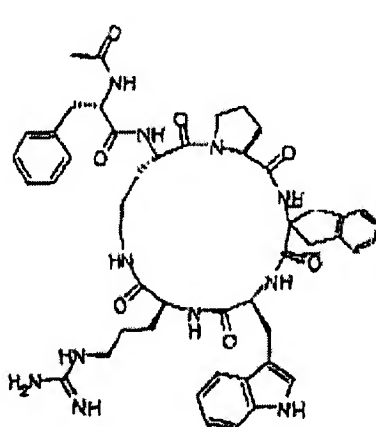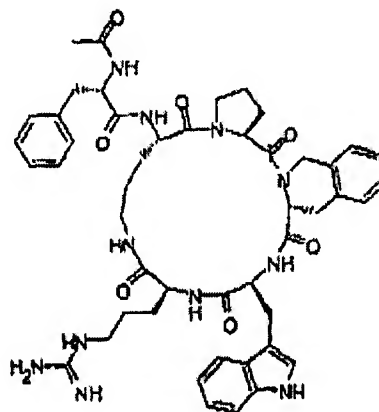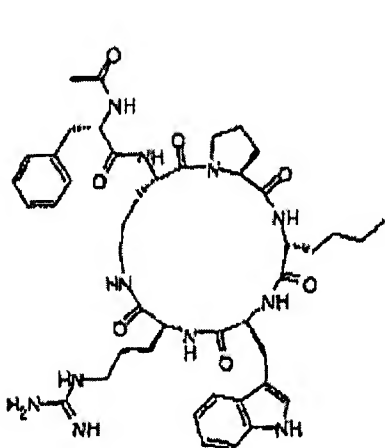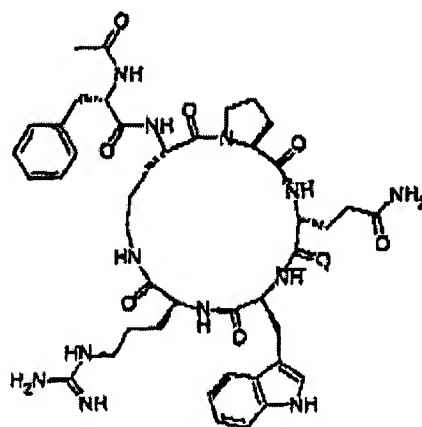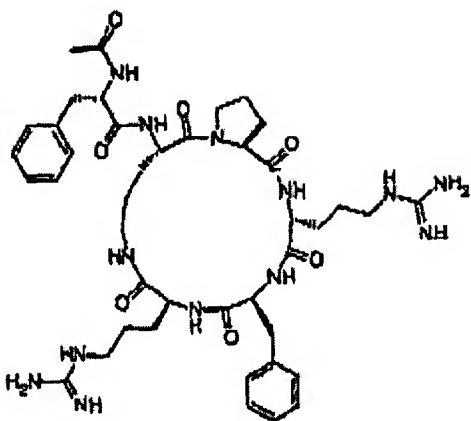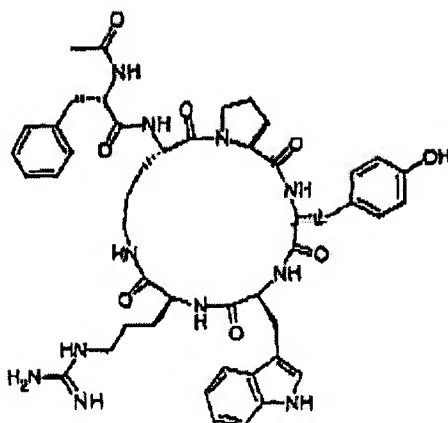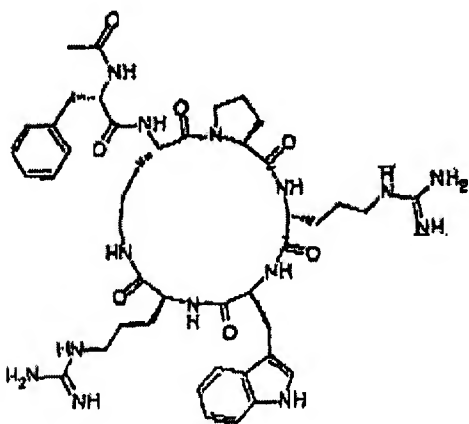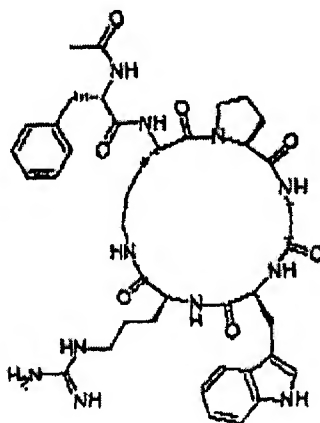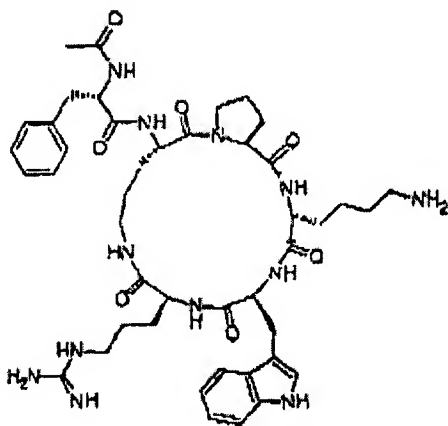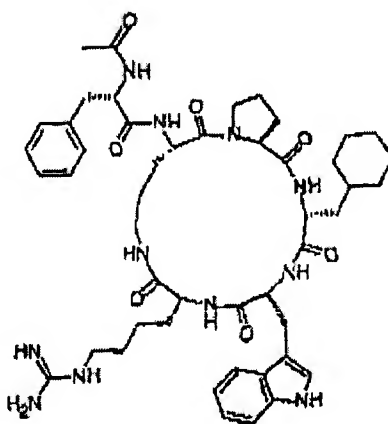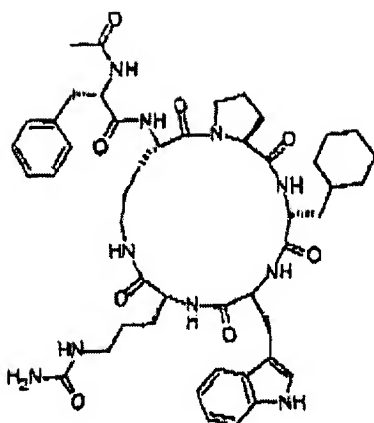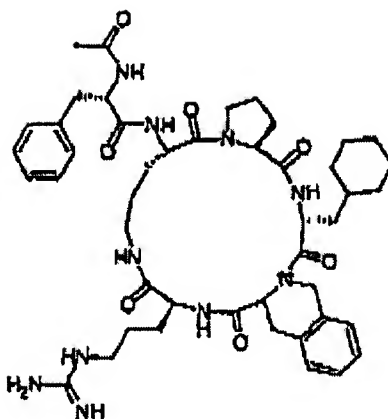
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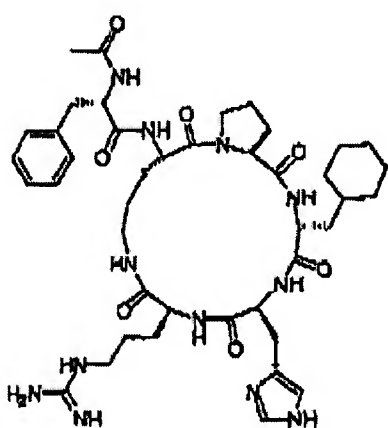
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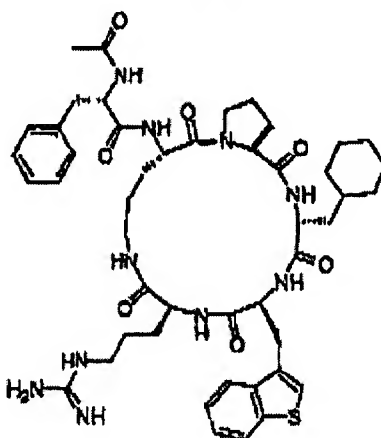
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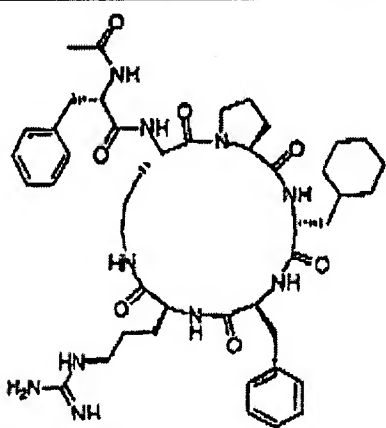
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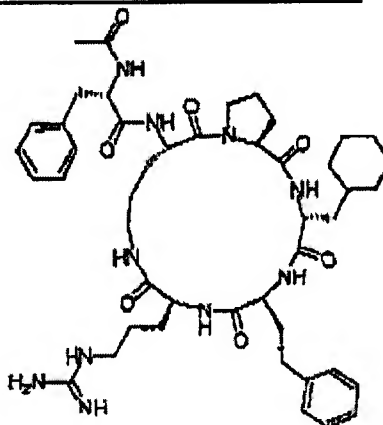
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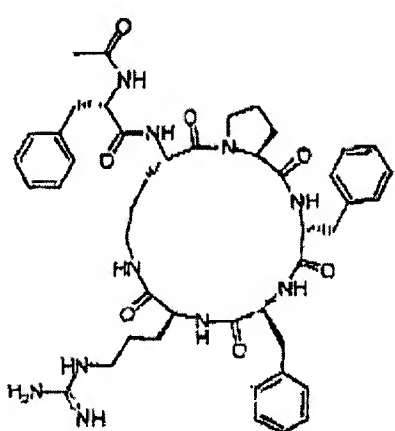
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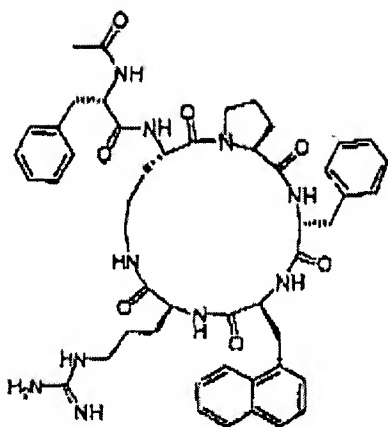
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14.   (Currently Amended)   The method of claim 13, in which the compound is compound **1**

(AcF-[OP-DCha-WR]), compound **33** (AcF-[OP-DPhe-WR]), compound **60** (AcF-[OP-

DCha-FR]) or compound **45** (AcF-[OP-DCha-WCit]):~~described in PCT/AU02/01427~~.
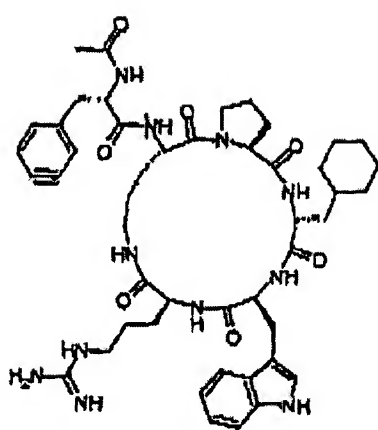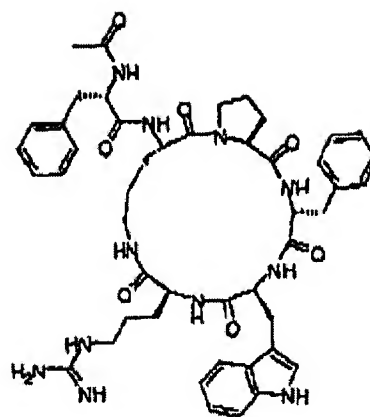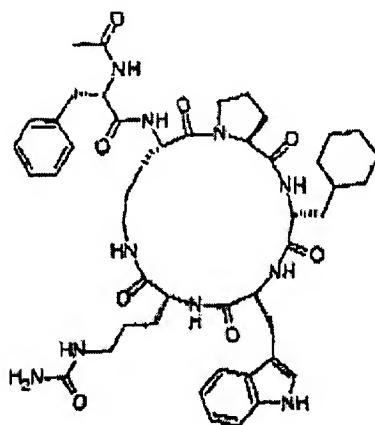
15. (Previously Presented) The method of claim 1, in which the inhibitor is used in conjunction with one or more other agents for the treatment of osteoarthritis.

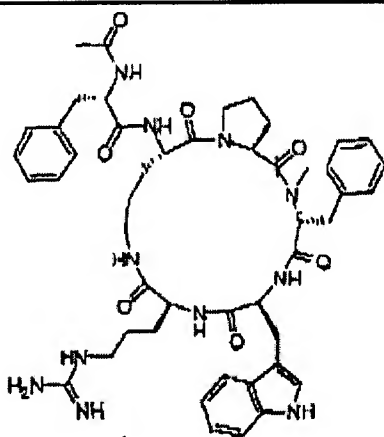16. (Previously Presented) The method of claim 1, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of

D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and **X^1** is -(CH$_2$)$_n$NH-, where *n* is 3.

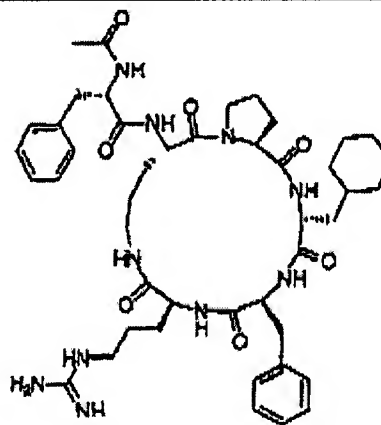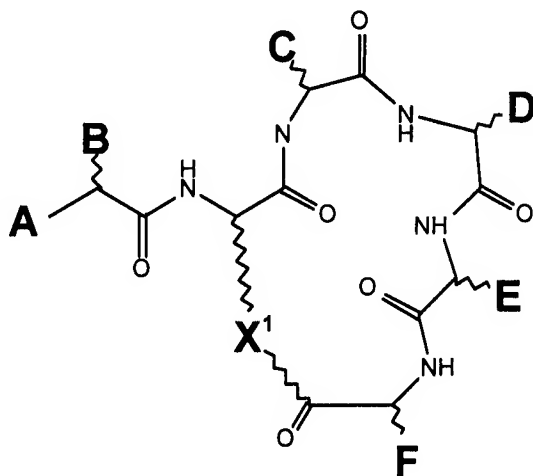17.   (Currently Amended)   A method for treating osteoarthritis in a mammal, said method comprising at least the step of: administering to a mammal in need thereof, an effective amount of a composition comprising a C5a G protein-coupled receptor antagonist compound that (a) has substantially no agonist activity and (b) is a cyclic peptide or peptidomimetic compound of General Formula formula I:

General Formula I(I)

wherein:

A is H, alkyl, aryl, NH$_2$, NH-alkyl, N(alkyl)$_2$, NH-aryl, NH-acyl, NH-benzoyl, NHSO$_3$, NHSO$_2$-alkyl, NHSO$_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B** <u>is</u> the side chain of ~~a D-~~ ~~or L-amino acid, but is not the side chain of glycine, D-phenylalanine,~~ ~~L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine~~ <u>L-phenylalanine or L-phenylglycine;</u>

C is the side chain of ~~a D-, L- or homo-amino acid, but is not the side chain of isoleucine,~~ ~~phenylalanine, or cyclohexylalanine~~ <u>glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline;</u>

D is the side chain of ~~a neutral D-amino acid, but is not the side chain of glycine or~~ ~~D-alanine, a bulky planar side chain, or a bulky charged side chain~~ <u>D-leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;</u>

E is ~~a bulky substituent, but is not~~ the side chain of ~~D-tryptophan, L-N-methyltryptophan,~~ ~~L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine,~~ ~~D-leucine, L-fluorenylalanine, or L-histidine~~<u>an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-napthyl or L-3-benzothienyl alanine;</u>

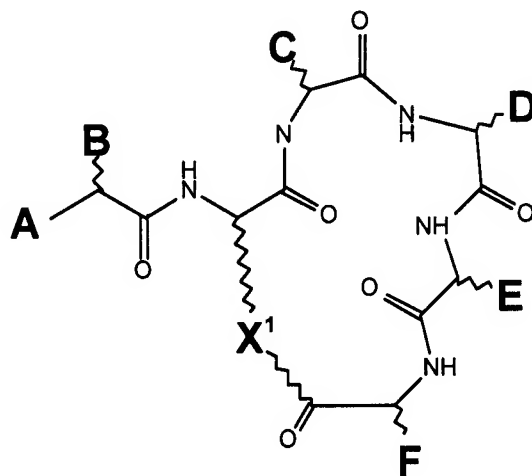**F** is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X^1 is -(CH$_2$)$_n$NH- or (CH$_2$)$_n$S-, where n is an integer of from 1 to 4; -(CH$_2$)$_2$O-;

-(CH$_2$)$_3$O-; -(CH$_2$)$_3$-; -(CH$_2$)$_4$-; -CH$_2$COCHRNH-; or -CH$_2$-CHCOCHRNH-, where R is

the side chain of any common or uncommon amino acid.

18.   (Currently Amended) The method of claim 17, wherein

A is H, alkyl, aryl, NH$_2$, NH-alkyl, N(alkyl)$_2$, NH-aryl, NH-acyl, NH-benzoyl, NHSO$_3$,

NHSO$_2$-alkyl, NHSO$_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or **B is** the side chain of ~~a D-~~

~~or L-amino acid, but is not the side chain of glycine, D-phenylalanine,~~

~~L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine~~

L-phenylalanine or L-phenylglycine;

C is the side chain of ~~a D-, L- or homo-amino acid, but is not the side chain of isoleucine,~~

~~phenylalanine, or cyclohexylalanine~~ glycine, alanine, leucine, valine, proline,

hydroxyproline, or thioproline;

D is the side chain of ~~a neutral D-amino acid, but is not the side chain of glycine or~~

~~D-alanine, a bulky planar side chain, or a bulky charged side chain~~ D-leucine,

D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine,

D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine;

E is ~~a bulky substituent, but is not~~ the side chain of ~~D-tryptophan, L-N-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine~~an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-napthyl or L-3-benzothienyl alanine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine; and

X^1 is -$(CH_2)_nNH$- or $(CH_2)_nS$-, where n is an integer from 1 to 4.

19.   (Previously Presented)   The method of claim 18, wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and X^1 is -$(CH_2)_nNH$-, where n is 3.

20.   (Currently Amended)   A method of treatment of osteoarthritis, said method comprising ~~at least~~ the step of administering to a subject in need thereof, an effective amount of a

pharmaceutically-acceptable composition that comprises a <u>C5a</u> G protein-coupled

receptor inhibitor, wherein said inhibitor:

(a)   is an antagonist of a <u>C5a</u> G protein-coupled receptor;

(b)   has substantially no agonist activity; and

(c)   is a cyclic peptide or peptidomimetic compound of ~~General Formula~~
<u>Iformula I</u>:

~~General Formula I~~<u>(I)</u>

wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side

chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the

side chain of L-tryptophan; **F** is the side chain of L-arginine; and X^1 is

-$(CH_2)_n$NH-, where *n* is 3.

21.   (New) A method of treating osteoarthritis in a subject, said method comprising the step
of administering to said subject an effective amount of a cyclic peptide or peptidomimetic
compound selected from the group consisting of:

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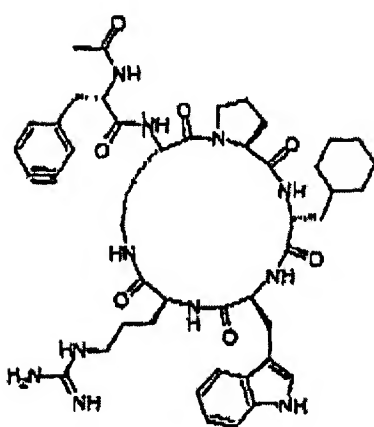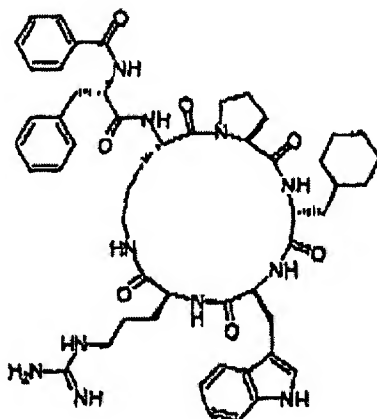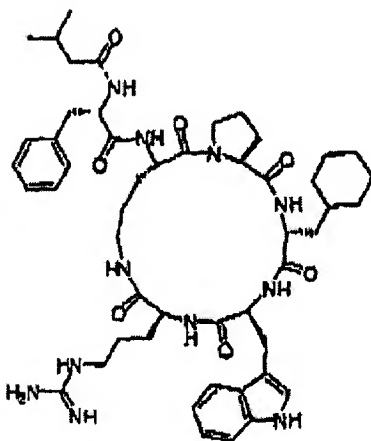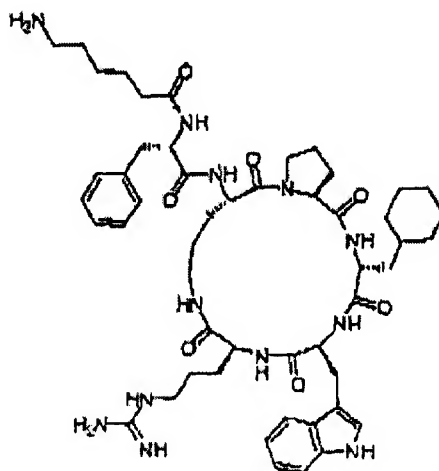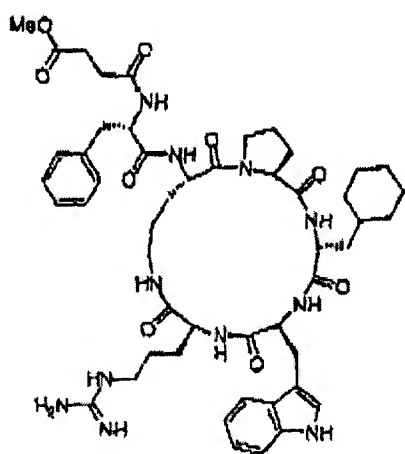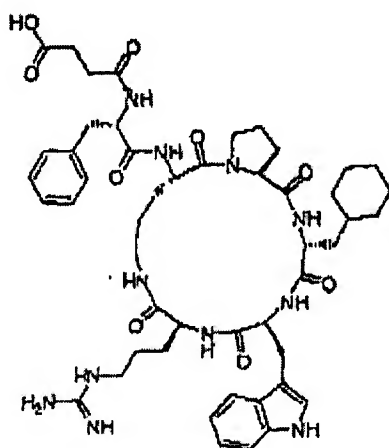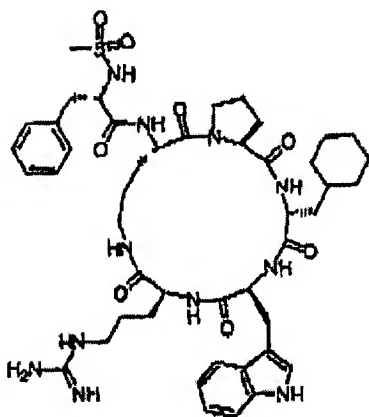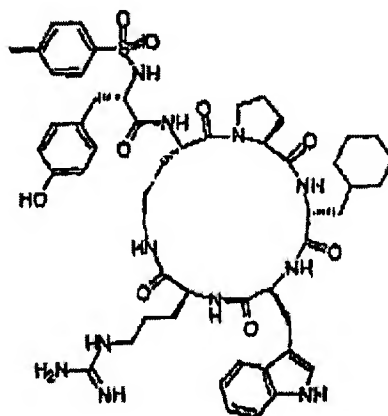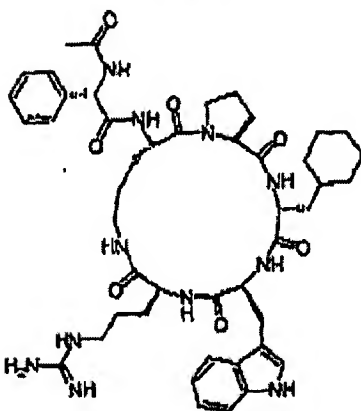
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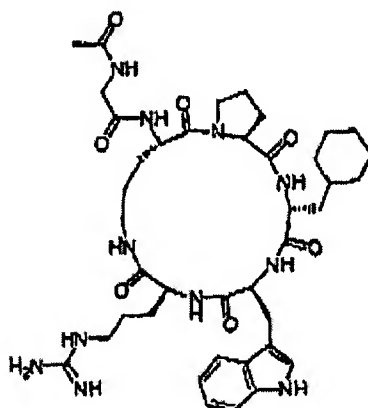
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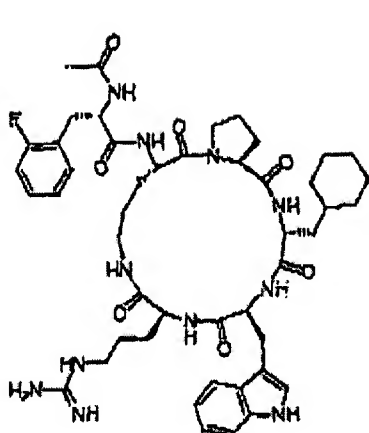
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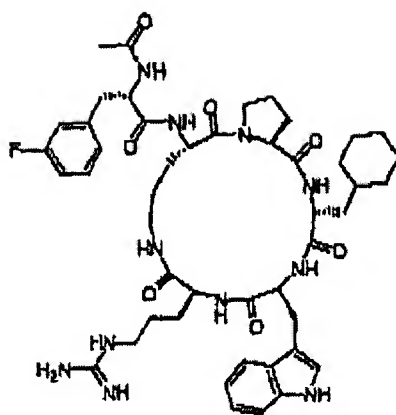
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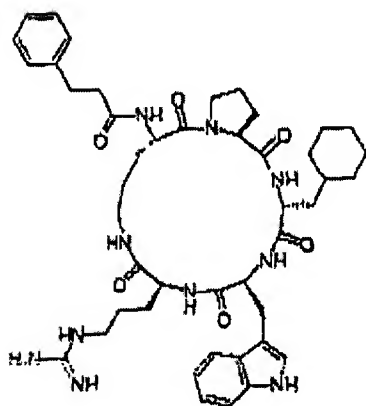
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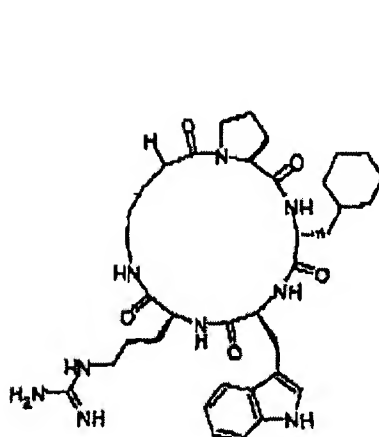
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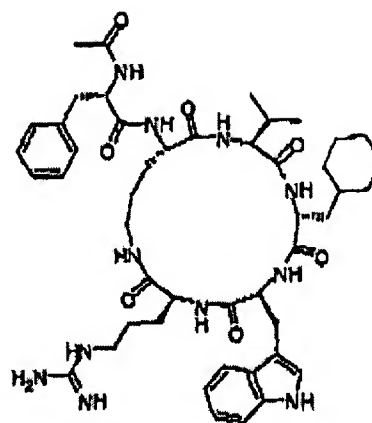
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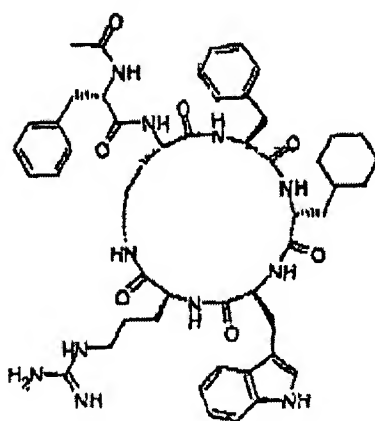
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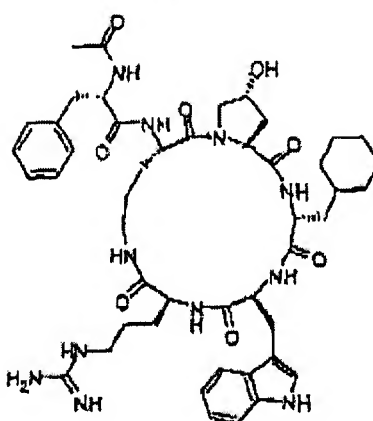
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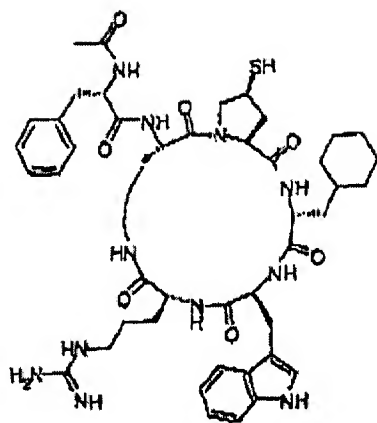
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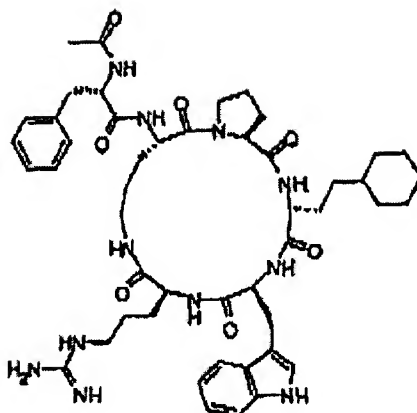
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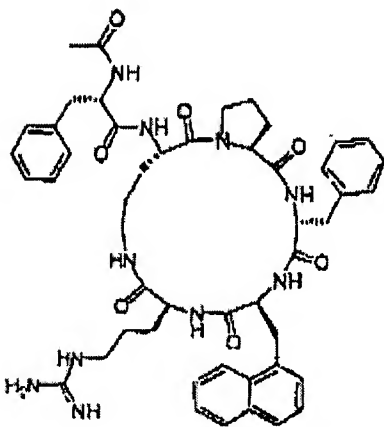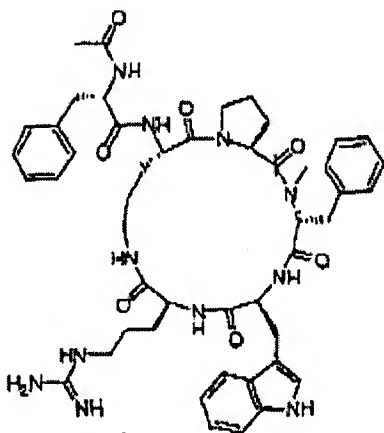57
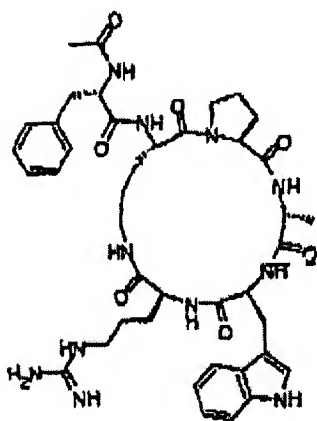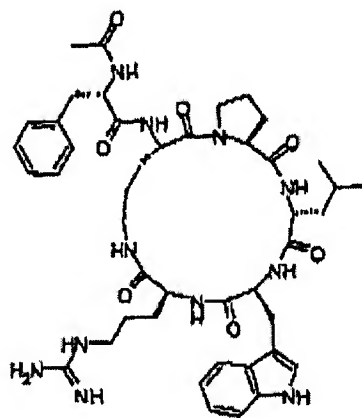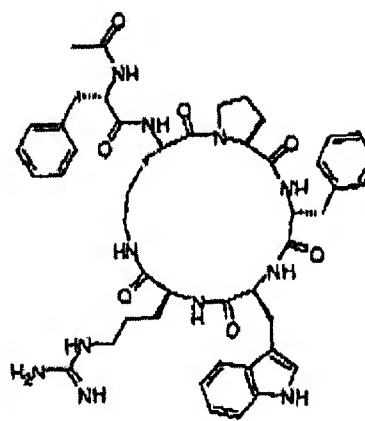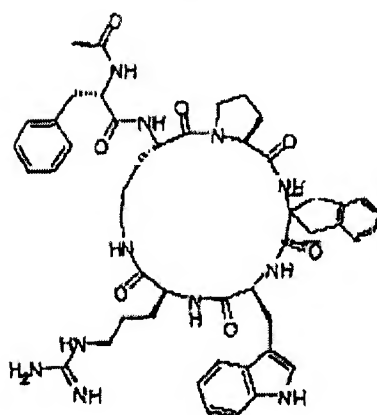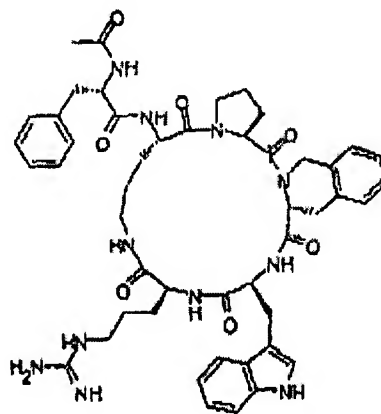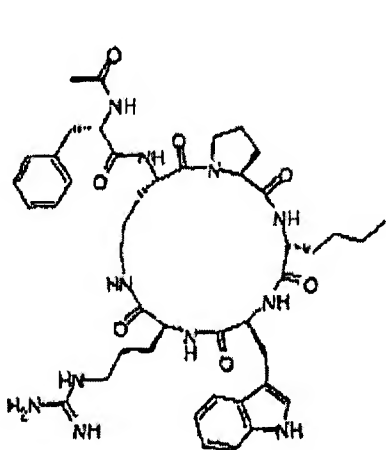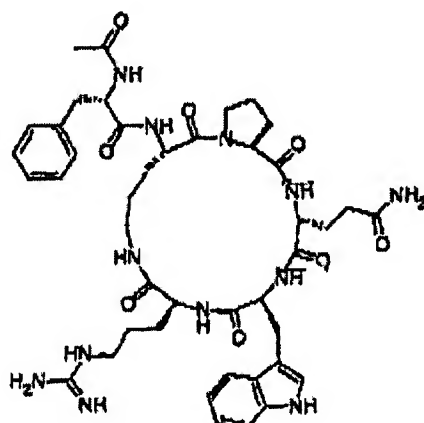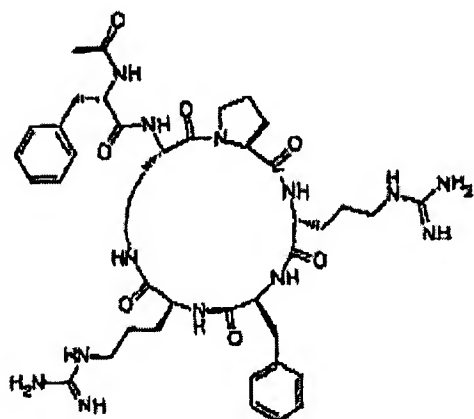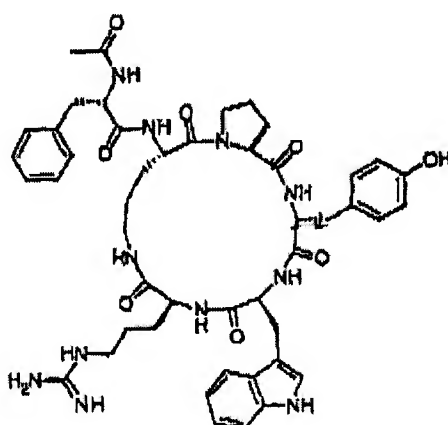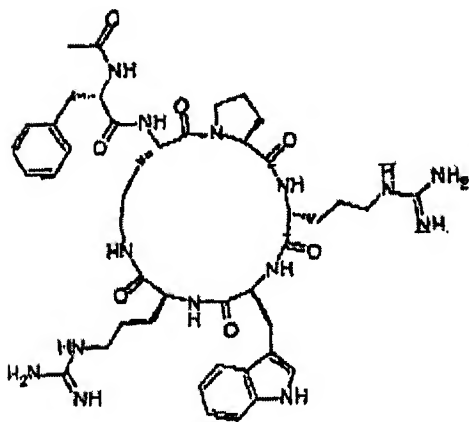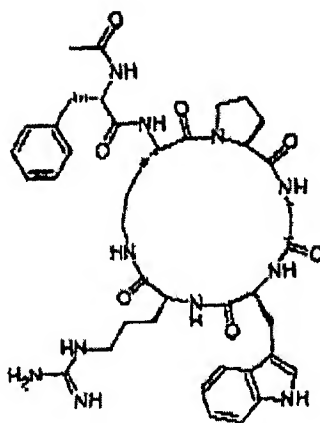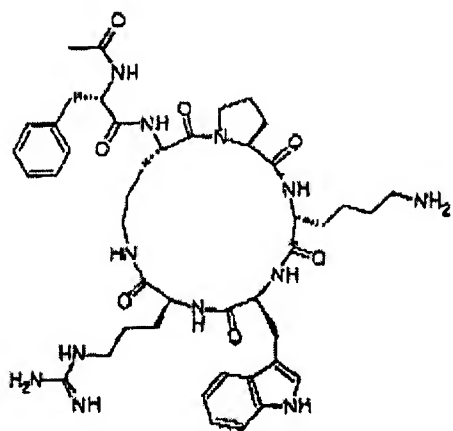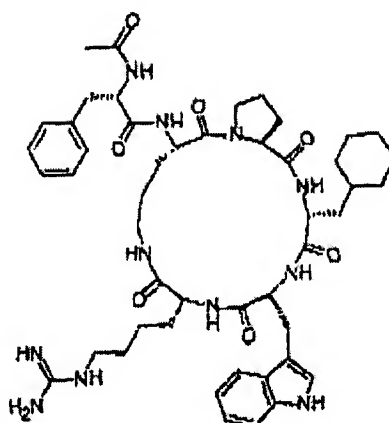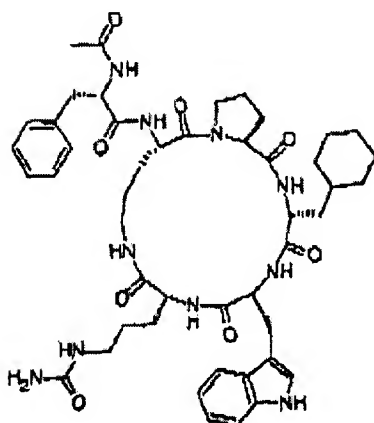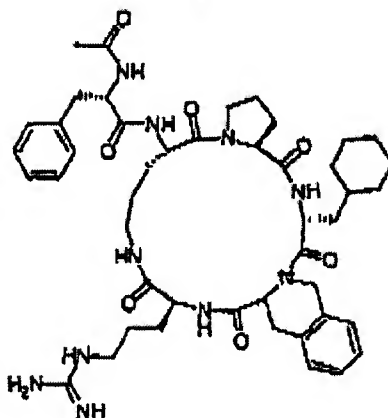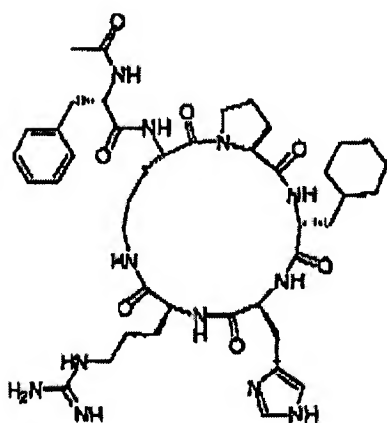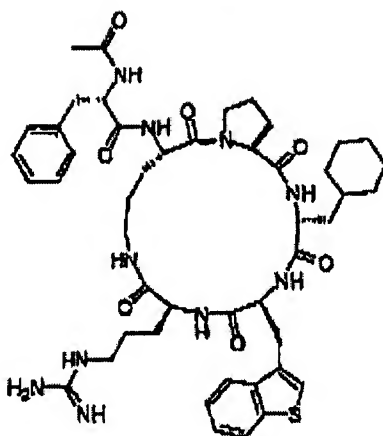
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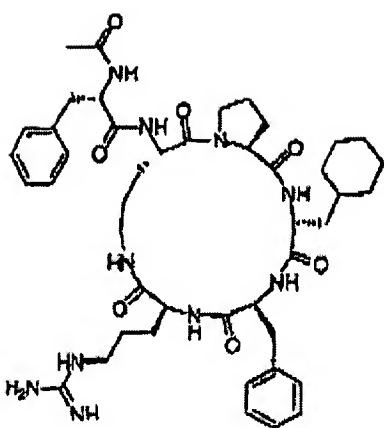
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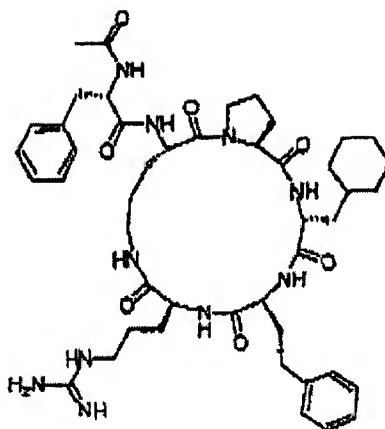
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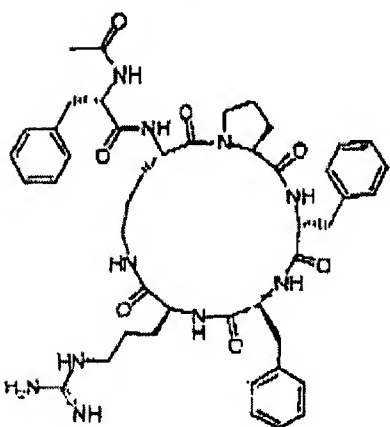
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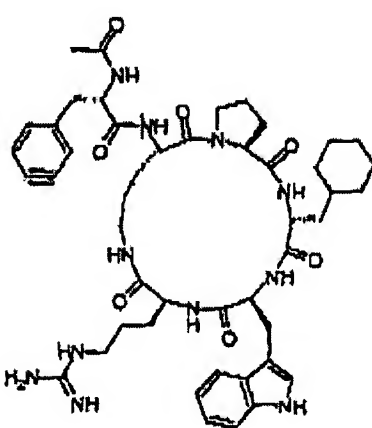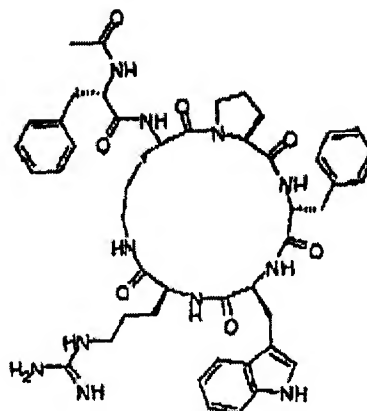
and

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wherein said compound is a C5a G protein-coupled receptor antagonist that has substantially no agonist activity.
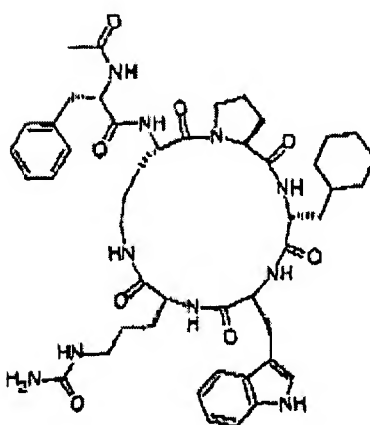
22.   (New)   The method of claim 21, wherein said compound is selected from the group consisting of:
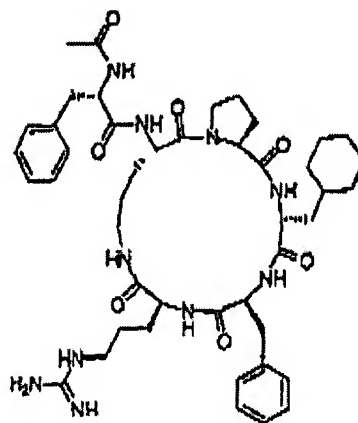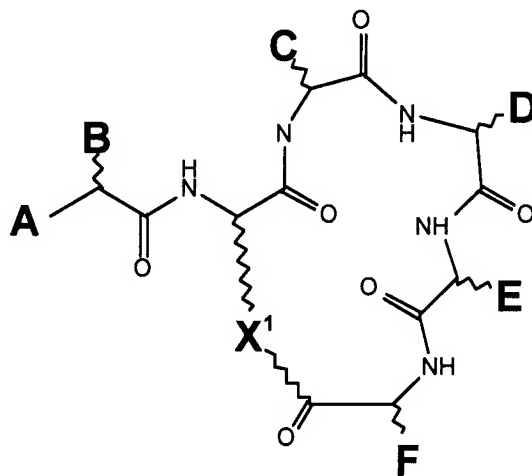

and

23. (New) A method for treating osteoarthritis in a mammal, said method comprising the step of: administering to a mammal in need thereof, an effective amount of a composition comprising a C5a G protein-coupled receptor antagonist compound that (a) has substantially no agonist activity and (b) is a cyclic peptide or peptidomimetic compound of formula I:

(I)

wherein **A** is NH-acyl; **B** is the side chain of L-phenylalanine; **C** is the side chain of L-proline; **D** is the side chain of D-cyclohexylalanine; **E** is the side chain of L-tryptophan; **F** is the side chain of L-arginine; and $\mathbf{X^1}$ is -$(CH_2)_n$NH-, where n is 3.